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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,876	UBER ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-141 and 143* is/are pending in the application.

4a) Of the above claim(s) *42-139* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-41,140,141 and 143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/10/10 has been entered.

Previous Claims and Rejections Status

2. Claims 1-4,6-141 and 143 are pending in the application. Claims 42-139 are withdrawn from consideration.

3. The rejection of claims 1-4,6-18,20-25,27-31,36-39,140,141 and 143 under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) is maintained.

4. The rejection of claims 1-4,6-25,27-31,36-39,140,141 and 143 under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) and in further view of Quay et al. (WO 96/40282) is maintained.

5. The rejection of claims 1-4,6-18,20-40,140,141 and 143 under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) in further view of Daum et al. (US 6,231,513) and Engel (EP0135822) is maintained.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-4,6-18,20-25,27-31,36-39,140,141 and 143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098).

8. Rossling et al. (US 6,468,506B1) discloses a system/apparatus for the production of gaseous microparticles/bubble medium for ultrasound diagnosis (i.e. imaging procedure) and the process for the production of gaseous microparticles (abstract; column 1, lines 7-12; figures). The apparatus comprises a tank **(17)** (i.e. reservoir for storing a liquid) which may be filled with gas via a valve **(2)**, line/gas flow path **(30)** and a pump **(16)** and/or liquid gas pump **(4)** (column 5, lines 5-33). The bubble generator, having an inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active substance solution, applying a vacuum and mixing with a stirring mechanism (i.e. means for disrupting an interface) between the liquid and the gas, not excluding multiple small wires or disks (column 2, lines 35-53).

9. An alternative method for the production of gaseous microparticles involves spraying the solution via a nozzle **(118)** into a column of gas where a pump **(16)** moves

the solution from a tank via nozzle into a line, heat exchanger **(15)** and column of gas **(12)**, etc. (column 3, lines 22-56). The size of the resulting particles may be controlled by the nozzle size, shape, type (not excluding those of the instant claims) as well as the working pressure and temperature in the column (column 3, lines 22-56).

10. Figure 1 shows the apparatus for the production of gaseous microparticles. It is also disclosed that a resuspended solution of gaseous microparticles may be filtered immediately before injection into a patient to increase the reliability (column 3, lines 60+; column 4, lines 13-15). The gaseous microparticles/bubble medium encompasses the gaseous microparticles/bubble medium of the instant claims and thus is capable of being generated for real time administration. Further, the recitation of real time does not exclude the time it takes for the system/apparatus to generate the microparticles/bubble medium.

11. Rossling et al. does not disclose a medium delivery system for direct injection into a patient or an imaging unit.

12. Uber, III et al. (US 6,397,098) discloses a system for producing a contrast-enhanced medical image of a patient including a source of a contrast or enhancement medium; a pressurizing unit in fluid connection with the source of contrast or enhancement medium; an imaging unit and a control unit (abstract; column 2, lines 22-45; column 5, lines 29-47). Communication between devices of the present invention is enabled through use of a control/communication interface to which each of the devices of the imaging/injection system can be connected (column 4, lines 13-24; column 5, lines 48-61). The interface can also be used to terminate an injection (i.e. verification

device) (column 14, lines 9-29). The system of the disclosure includes a concentration regulator (i.e. verification device) which selectively destroys microbubbles (column 8, lines 56-65). The concentration regulator also encompasses the filter of the instant claims as it removes bubbles, not excluding those having a diameter greater than a predetermined size. The contrast or enhancement medium being gas filled microspheres containing a therapeutic agent or is also called the fluid medium, being a liquid, gas or solid suspended in a liquid or a gas. The imaging unit provides (preferably in real-time) an indication (for example, a visual or audible indication) of an internal state, condition or view of the patient based upon a signal resulting from the energy applied to the region of a patient. The pressurizing unit is in fluid connection with the source of fluid medium to pressurize the fluid medium for injection into the patient (column 3, lines 38-52).

13. Uber, III et al. also discloses the method for adjusting the condition of a fluid medium, described above, during an imaging procedure (column 4, lines 57+). The control unit is adapted to adjust the conditions (i.e. contrast medium concentration, flow rate of the contrast medium, etc.) of the contrast or enhancement medium in the patient based upon the signal resulting from the energy applied to the region of the patient. The system may include general components or pieces of equipment, i.e. injector, etc (column 2, lines 22-53; column 3, lines 65+; column 4, lines 26-50).

14. At the time of the invention it would have been obvious to one ordinarily skilled in the art to create gaseous microparticles with the apparatus of Rossling et al. and administer them to a patient with the injector system of Uber, III et al. for direct

administration of the contrast agent to a patient as Uber, III et al. teaches that the pressurizing unit of the system (Uber, III et al.) is in fluid connection with the source of fluid medium (contrast or enhancement medium) to pressurize the fluid medium for the advantage of direct injection into the patient. Uber, III et al. also teaches that the system may include general components or pieces of equipment manufactured by more than one company (Uber, III et al. column 2, lines 42-45), not excluding the system for generating microbubbles of Rossling et al.

15. Also, one would have a reasonable expectation of success for introducing a plurality of gases via inlets in the system/apparatus of Rossling et al. to vary/enhance the desired microbubble composition.

16. Claims 1-4,6-25,27-31,36-39,140,141 and 143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) and in further view of Quay et al. (WO 96/40282).

17. Rossling et al. (US 6,468,506B1) discloses a system/apparatus for the production of gaseous microparticles/bubble medium for ultrasound diagnosis (i.e. imaging procedure) and the process for the production of gaseous microparticles as well as that stated above. Rossling et al. does not disclose a medium delivery system for direct injection into a patient comprising an imaging unit or the production of microbubbles via the introduction of solid particles.

18. Uber, III et al. (US 6,397,098) discloses a system for producing a contrast-enhanced medical image of a patient includes a source of a contrast or enhancement

medium; a pressurizing unit in fluid connection with the source of contrast or enhancement medium; an imaging unit and a control unit as well as that stated above.

19. Quay et al. (WO 96/40282) discloses the enhance production of gaseous microbubbles via the introduction of solid particles in the gas-liquid emulsion where there is a significant increase in bubble population per unit volume (abstract; p6, lines 7-12; p8, lines 7-25). The activation process of the disclosure provides for enhancement of the contrast in an ultrasound image generated during medical diagnosis (p4, lines 4-11).

20. At the time of the invention it would have been obvious to one ordinarily skilled in the art to create microparticles with the apparatus of Rossling et al. and administer them to a patient with the injector system of Uber, III et al. for direct administration of the contrast agent to a patient as Uber, III et al. teaches that the pressurizing unit of the system (Uber, III et al.) is in fluid connection with the source of fluid medium (contrast or enhancement medium) to pressurize the fluid medium for the advantage of direct injection into the patient. Uber, III et al. also teaches that the system may include general components or pieces of equipment manufactured by more than one company (Uber, III et al. column 2, lines 42-45), not excluding the system for generating microbubbles of Rossling et al.

21. Also, one would have a reasonable expectation of success for introducing a plurality of gases via inlets in the system/apparatus of Rossling et al. to vary/enhance the desired microbubble composition.

22. At the time of the invention it would have been obvious to one ordinarily skilled in the art to generate microparticles via nucleation with solid particles as it is a known technique in the art for generating gaseous microparticles with significant increase in bubble population per unit volume and thus provides enhanced imaging.

23. Claims 1-4,6-18,20-40,140,141 and 143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) in further view of Daum et al. (US 6,231,513) and Engel (EP0135822).

24. Rossling et al. (US 6,468,506B1) discloses a system/apparatus for the production of gaseous microparticles/bubble medium for ultrasound diagnosis (i.e. imaging procedure) and the process for the production of gaseous microparticles as well as that stated above. Rossling et al. does not disclose a medium delivery system for direct injection into a patient comprising an imaging unit or the production of microbubbles via ultrasound/introduction of a plate.

25. Uber, III et al. (US 6,397,098) discloses a system for producing a contrast-enhanced medical image of a patient includes a source of a contrast or enhancement medium; a pressurizing unit in fluid connection with the source of contrast or enhancement medium; an imaging unit and a control unit as well as that stated above.

26. Daum et al. (US 6,231,513) discloses a microbubble forming arrangement having a plurality of microholes which when a gas is passed through causes the gas to form numerous microbubbles in fluid (column 3, lines 1-6). The microbubble forming arrangement includes multi-perforated membrane (two dimensional material that

includes microholes) or porous matrix (three dimensional structure which includes microholes) (column 3, lines 7-24). The microbubble forming arrangement may be formed from polytetrafluoroethylene, polyethylene, ceramic, sintered alloy, etc. (column 3, lines 7-23). Daum et al. also discloses the use of piezoelectric ultrasound for the preparation of gas-filled microbubbles used for ultrasound diagnosis (column 4, lines 10-24).

27. Engel (EP0135822) discloses a diffusor (plate) or a series-arrangement for the throughpassage of a fluid having a multitude of channels which extend therethrough in a mutually parallel relationship (abstract). The diffuser enables a particularly uniform distribution of the fluid over large surface areas (p1, lines 24-28) and the generation of a stream of fine bubbles (p4, lines 1-8). The permeable plate may further comprise a water-permeable layer for draining purposes (p2, lines 25-30; p4, lines 9-24).

28. At the time of the invention it would have been obvious to one ordinarily skilled in the art to create microparticles with the apparatus of Rossling et al. and administer them to a patient with the injector system of Uber, III et al. for direct administration of the contrast agent to a patient as Uber, III et al. teaches that the pressurizing unit of the system (Uber, III et al.) is in fluid connection with the source of fluid medium (contrast or enhancement medium) to pressurize the fluid medium for the advantage of direct injection into the patient. Uber, III et al. also teaches that the system may include general components or pieces of equipment manufactured by more than one company (Uber, III et al. column 2, lines 42-45), not excluding the system for generating microbubbles of Rossling et al.

29. Also, one would have a reasonable expectation of success for introducing a plurality of gases via inlets in the system/apparatus of Rossling et al. to vary/enhance the desired microbubble composition.

30. At the time of the invention it would have been obvious to one ordinarily skilled in the art to generate microparticles via piezoelectric ultrasound as it is a known technique in the art for generating gaseous microparticles with significant increase in bubble population per unit volume and thus provides enhanced imaging.

Response to Arguments

31. Applicant's arguments filed 5/10/10 have been fully considered but they are not persuasive.

32. Applicant asserts that the combination of the references of Rossling et al. and Uber, III et al. would only yield a bubble contrast medium formed by adding water to the pre-packaged (dried, spherically-shaped, gas-containing) microparticles of Rossling et al. to rehydrate same and a syringe filled with that bubble contrast medium placed into the system of Uber, III et al. After the syringe containing the reconstituted/rehydrated bubble medium is loaded into the system of Uber, III et al., the combination would result in the same system as that taught in the Uber, III et al. patent itself, specifically, a system that is only capable of reducing the concentration of bubbles in the medium to a desired level.

33. The reference of Rossling et al. was used to teach a system/apparatus for the production of gaseous microparticles/bubble medium comprising components which

encompass the system of the instant claims, such as tank **(17)** (i.e. reservoir for storing a liquid); pump **(16)** and/or liquid gas pump **(4)**; inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active substance solution; vacuum; stirring mechanism (i.e. means for disrupting an interface), etc.

34. The system/apparatus of Rossling et al. generate microparticles/bubble medium in real time as the recitation of real time in the instant claims does not exclude the time it takes for the system/apparatus to generate the microparticles/bubble medium.

35. The reference of Uber, III. et. al. was used to teach of a system for producing a contrast-enhanced medical image of a patient including a source of a contrast or enhancement medium; a pressurizing unit in fluid connection with the source of contrast or enhancement medium an imaging unit and a control unit and the method for adjusting the condition of a fluid medium during an imaging procedure. The control unit is adapted to adjust the conditions (i.e. contrast medium concentration, flow rate of the contrast medium, etc.) of the contrast or enhancement medium in the patient based upon the signal resulting from the energy applied to the region of the patient. The system may include general components or pieces of equipment, i.e. injector, etc.

36. At the time of the invention it would have been obvious to one ordinarily skilled in the art to create microparticles with the apparatus of Rossling et al. and administer them to a patient with the injector system of Uber, III et al. for direct administration of the contrast agent to a patient as Uber, III et al. teaches that the pressurizing unit of the system (of Uber, III et al.) is in fluid connection with the source of fluid medium (contrast or enhancement medium) to pressurize the fluid medium for the advantage of direct

injection into the patient. Uber, III et al. also teaches that the system may include general components or pieces of equipment manufactured by more than one company (Uber, III et al. column 2, lines 42-45), not excluding the system for generating microbubbles of Rossling et al.

37. Further, the instant claims teach that the operating parameter being controlled by the controller may be the concentration of bubbles in the medium, rate of flow of the medium, etc. which is encompassed by the adjustment of the contrast medium concentration, flow rate of the contrast medium, etc. by the control unit of Uber, III et al.

38. Applicant asserts that the references of Rossling et al. and Uber, III et al. teach of a system which is incapable of increasing the concentration of bubbles to a higher level on the fly should the need to do so arise.

39. The instant claims do not recite increasing the concentration of bubbles to a higher level but does recite that the fluid verification device for monitoring and changing at least one operating parameter, such as contrast medium concentration, flow rate of the contrast medium, etc. The instant claims further recite that the fluid verification device is capable of destroying any of the bubbles having a diameter at least one of greater than, less than, within, and outside of a predetermined range of sizes.

40. Uber, III et al. teaches that the control unit is adapted to adjust the conditions (i.e. contrast medium concentration, flow rate of the contrast medium, etc.) of the contrast or enhancement medium in the patient based upon the signal resulting from the energy applied to the region of the patient.

41. Applicant asserts that Rossling et al. does not disclose a system whose controller enables an operator to "adjust in real time parameters... pertaining to generation and/or delivery into the patient of the medium inclusive of the properties of the bubbles therein" for the purpose stabilizing and/or optimizing a medical (e.g. imaging) procedure being performed on the patient.

42. The reference of Rossling et al. was not used to teach of the adjustment in real time of the parameters but was used to teach of a system/apparatus for the production of gaseous microparticles/bubble medium comprising components which encompass the system of the instant claims, such as tank **(17)** (i.e. reservoir for storing a liquid); pump **(16)** and/or liquid gas pump **(4)**; inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active substance solution; vacuum; stirring mechanism (i.e. means for disrupting an interface), etc.

43. The system/apparatus of Rossling et al. generate gaseous microparticles/bubble medium in real time as the recitation of real time in the instant claims does not exclude the time it takes for the system/apparatus to generate the gaseous microparticles/bubble medium.

44. The reference of Uber, III. et. al. was used to teach of a system for producing a contrast-enhanced medical image of a patient including a source of a contrast or enhancement medium; a pressurizing unit in fluid connection with the source of contrast or enhancement medium; an imaging unit and a control unit and the method for adjusting the condition of a fluid medium during an imaging procedure. The control unit is adapted to adjust the conditions (i.e. contrast medium concentration, flow rate of the

contrast medium, etc.) of the contrast or enhancement medium in the patient based upon the signal resulting from the energy applied to the region of the patient. The system may include general components or pieces of equipment, i.e. injector, etc.

45. Therefore, it would have been obvious to one ordinarily skilled in the art to administer the gaseous microparticles/bubble medium of Rossling et al. to a patient with the injector system of Uber, III et al. for direct administration of the contrast agent to a patient as Uber, III et al. teaches that the pressurizing unit of the system (of Uber, III et al.) is in fluid connection with the source of fluid medium (contrast or enhancement medium) to pressurize the fluid medium for the advantage of direct injection into the patient and the system may include general components or pieces of equipment manufactured by more than one company (Uber, III et al. column 2, lines 42-45), not excluding the system for generating microbubbles of Rossling et al.

46. Thus, the injector system of Uber, III et al. allows for adjustments to the conditions (i.e. contrast medium concentration, flow rate of the contrast medium, etc.) of the contrast or enhancement medium in the patient based upon the signal resulting from the energy applied to the region of the patient.

Conclusion

47. No claims are allowed at this time.

48. This is a continuation of applicant's earlier Application No. 10/798,876. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had

been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

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Examiner, Art Unit 1618